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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHUNG, SUSANNAH LEE	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 11/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,627	RUKHMAN ET AL.	
	Examiner	Art Unit	
	Susannah Chung	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8,9,12-14,17 and 81-94* is/are pending in the application.

4a) Of the above claim(s) *1,3-6,8,9,12-14,81,82 and 84-94* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20060717*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The instant application is a Request for Continued Examination (RCE). Claims 1, 3-4, 5-6, 8-9, 12-13, 14, 17, 81-93 and 94 are pending in the instant application. Claims 2, 7, 10-11, 15, 16, 18, 19-79 and 80 are canceled. Claims 83-94 are new.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 3, 4, 5, 6, 12 and 13 drawn to a process for preparing amorphous form of valsartan comprising the steps of: a) precipitating amorphous valsartan from a solution of valsartan in methyl t-butyl ether, ethanol, DMF, acetone, etc...; and b) recovering valsartan amorphous form, wherein the amorphous form has a DSC thermogram that lacks a melting enthalphy above above 1 J/g.

II. Claims 8 and 9 drawn to a process for preparing amorphous form of valsartan comprising the steps of: a) suspending valsartan in a solvent selected from the group consisting of water and C.sub.5 to C.sub.12 saturated hydrocarbon to obtain amorphous valsartan; and b) recovering the amorphous valsartan.

III. Claim 14 drawn to a process for preparing amorphous form of valsartan comprising the steps of: a) heating valsartan in diisopropyl ether to obtain amorphous valsartan; and b) recovering the amorphous valsartan.

IV. Claims 17 and 83 drawn to an amorphous form of valsartan, wherein the amorphous form has a DSC thermogram that lacks a melting point above about 1 J/g.

V. Claims 81 and 93 drawn to a pharmaceutical composition comprising amorphous valsartan of claim 17, and a pharmaceutically acceptable excipient.

VI. Claims 82 and 94 drawn to a method for treating hypertension comprising the step of administering the pharmaceutical composition of claim 81 to the mammal in need thereof.

VII. Claims 84-87 and 90-91 drawn to a process for preparing amorphous form of valsartan comprising the steps of: a) precipitating amorphous valsartan from a mixture of water and a solvent selected from the group consisting of ethanol, DMF, acetone, and mixtures thereof; and b) recovering the precipitated amorphous valsartan, wherein the amorphous form has a DSC thermogram lacks a melting enthalpy above about 1 J/g in region of about 80°C to about 100°C in said DSC.

VIII. Claims 88 and 89 are drawn to a process for preparing amorphous form of valsartan comprising the steps of: a) suspending valsartan in water to obtain amorphous valsartan; and b) recovering the amorphous valsartan, wherein the amorphous form has a DSC thermogram that lacks a melting enthalpy above about 1 J/g in region of about 80°C to about 100°C in said DSC.

This list is not exhaustive as it would be impossible under the time constraints due to the sheer volume of subject matter instantly claimed. Therefore, applicant may choose to elect a single invention (a product or a method of use of said product) by identifying another specific embodiment, i.e. another process of making amorphous valsartan or a different form of valsartan,

etc..., not listed in the exemplary groups of the invention and examiner will endeavor to group the same.

Rationale Establishing Patentable Distinctiveness Within Each Group

Each Group listed above is directed to or involves the use of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP 806.04, MPEP 808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over the other invention (Group), i.e. they are patentable over each other. Chemical structures, which are similar, are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrebuttable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holding of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

The above groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons:

Inventions I and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) that the process for using the product as claimed can be practiced with another materially different product or (2) that the

product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed in Group IV can be in materially different processes as shown in Groups I-III and VI-VIII.

Inventions I-III and VI-VIII represent separate and distinct processes of making a compound of formula (I). Processes are separate and distinct if they differ with respect to starting materials, reagents, and method steps. In the instant case, Inventions I-III and VI-VIII use different starting materials, reagents and method steps to yield the amorphous valsartan. Since, Inventions I-III and VI-VIII are separate and distinct process of making they have different issues regarding patentability and enablement and represent patentably distinct subject matter.

In addition, because of the different limitations in the claims and different classes and subclasses of the Inventions that must be search, a serious burden is imposed on the examiner to perform a complete search of the defined areas. Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden in the examination of this application.

Advisory of Rejoinder

The following is a recitation of M.P.E.P. 821.04, Rejoinder:

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02(c) and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims, which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.
>
> Where the application as originally filed discloses the product and the process for making and/or using the product, and only claims directed to the product are presented for examination, when a product claim is found allowable, applicant may present claims directed to the process of making and/or using the patentable product by way of amendment pursuant to 37 CFR 1.121. In view of the rejoinder procedure, and in order to expedite prosecution, applicants are encouraged to present such process claims, preferably

as dependent claims, in the application at an early stage of prosecution. Process claims, which depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance. Amendments submitted after final rejection are governed by 37 CFR 1.116. Process claims which do not depend from or otherwise include the limitations of the patentable product will be withdrawn from consideration, via an election by original presentation (see MPEP § 821.03). Amendments submitted after allowance are governed by 37 CFR 1.312. Process claims which depend from or otherwise include all the limitations of an allowed product claim and which meet the requirements of 35 U.S.C. 101, 102, 103, and 112 may be entered.

Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to 37 CFR 1.129(b), applicant may either: (A) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2); or (B) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)). Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined. If applicant chooses to pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2) even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26(a) states that "[T]he Commissioner may refund any fee paid by mistake or in excess of that required. A change of purpose after the payment of a fee...will not entitle a party to a refund of such fee..." In this case, the fees paid under 37 CFR 1.129(b) were not paid by mistake nor paid in excess, therefore, applicant would not be entitled to a refund. In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101,102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action. Form paragraphs 8.42 through 8.44 should be used to notify applicant of the rejoinder of process claims which depend from or otherwise include all the limitations of an allowable product claim.

In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

"However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all the limitations of** an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

Therefore, in accordance with M.P.E.P. 821.04 and In re Ochiai, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are

allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

During a telephone conversation with Attorney Payam Moradian on October 26, 2006 a provisional election was made *with traverse* to prosecute the invention of Group IV, comprising Claims 17 and 83 drawn to an amorphous form of valsartan, wherein the amorphous form has a DSC thermogram that lacks a melting point above about 1 J/g. Affirmation of this election must be made by applicant in replying to this Office action.

Response to Remarks filed on September 12, 2006

I. Interview

An in-person interview was conducted on July 17, 2006 between Inventor Judith Aronhim, Attorney Payam Moradian, Supervisory Examiner Joseph McKane and Examiner Andrew Freistein (see enclosed interview summary form, paper date 20060717 and Remarks filed on 9/12/06, page 7, paragraph 1). It is acknowledged that Applicants agreed to file an RCE, re-introduce claim 18, and that claims 17 and 18 would have to be amended for clarity. In view of this, Applicants filed an amendment to the claims on September 12, 2006, where claim 17 was amended and claim 18 was amended as new claim 83.

II. Amendment of "melting point" to "melting enthalpy"

Applicants have amended the claims to recite "melting enthalpy" instead of "melting point." (See Remarks filed on 9/12/06, page 7, paragraph 3). The general rule is that no new

matter may be introduced into an application after its filing date. MPEP 601.01(b). In the instant application, the amendment from "melting point" to "melting enthalpy" is *not* deemed new matter due to the inherent or implicit teachings of the drawings and specification.

The applicable rule for interpreting the claims is that "each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." See MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). The specification, on page 18, second paragraph states that the "valsartan purely amorphous" has a DSC thermogram as substantially depicted in FIG. 3. The DSC thermogram lacks endothermic peaks, such as those above about 1 J/g, preferably those above about 0.5 J/g, in the region of from about 80°C. to about 100°C. This along with Applicants remarks suggest that the melting enthalpy was intended, not the melting point.

III. 35 U.S.C. 103(a) rejection

Claims 17 currently stands rejected under 35 U.S.C. 103(a) as being unpatentable over Buhlmayer et al., U.S. Pat. Num. 5,399,578 (Date of Patent: March 21, 1995). To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP 2143. In the instant case, a prima facie case of

obviousness has been established. (See 102 and 103 rejections below). A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). MPEP 2144.09. Applicants argue that there was no suggestion in the art on how to prepare amorphous valsartan lacking a melting enthalpy in the DSC, and there was no reasonable expectation of success of preparing such amorphous valsartan. (See Remarks, p. 9, 3rd paragraph). The instant application states different processes of making amorphous valsartan ranging from precipitating it out of solution, to recrystallization, to evaporating the solvent under reduced pressure (see specification, examples 1-19 and 20-31, page 25-30 and 32. The prior art of Bulhmayer discloses the same processes of preparing valsartan, (S)-N-(1-carboxy-2-methyl-prop-1-yl)-N-pentanoyl-N-[2'-(1H-tetrazol-5-yl)biphenyl-4-ylmethyl]-amine, and analogs of valsartan, wherein the valsartan or valsartan analogs are precipitated out of solution, recrystallized, evaporated out of solvent, etc.... (See Examples 1-91, columns 28-62. See Example 16, wherein the process of making valsartan is taught by flash chromatography, which one skilled in the art would know is followed by evaporation, either under reduced pressure or not. Also see Examples 23, 32, 51, 53, and 60, which all teach that the product precipitates out.)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17 and 83 are rejected under 35 U.S.C. 102(b) as being anticipated by Buhlmayer et al., U.S. Pat. Num. 5,399,578.

Applicants claims relate to an amorphous form of valsartan, wherein the amorphous form has a DSC thermogram that lacks a melting point above about 1 J/g and wherein the melting point is lacking in the region of from about 80°C to about 100°C. Buhlmayer discloses valsartan and its analogs, but is silent as to whether the amorphous form is present. Despite this, Applicants must show that their amorphous form really is different from any of the ones prepared in the prior art. In other words, would one skilled in the art, using the processes disclosed in the prior art be able to make the amorphous form, either purely amorphous or partially amorphous?

MPEP 2112 states: SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE UPON THE DIS-COVERY OF A NEW PROPERTY.

The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

In this case, the "unknown property" is the particular amorphous form. This is unknown because the reference is silent on this property.

MPEP 2112 goes on to state: INHERENT FEATURE NEED NOT BE RECOGNIZED AT THE TIME OF THE INVENTION.

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003). In SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005), the Federal Circuit held that a prior art patent to an anhydrous form of a compound "inherently" anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound "inherently results in at least trace amounts of" the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate.

Likewise, in the instant application, the valsartan claimed in the prior art "inherently" anticipated the claimed amorphous form of the compound because practicing the process in the prior art to manufacture the valsartan "inherently results in the at least trace amounts of" the claimed amorphous form even if the prior art did not discuss or recognize the amorphous form.

MPEP 2112 further states: A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC.

Where applicant claims a composition in terms of a function, property or characteristic

and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection.

Again, the characteristic which the prior art is silent on is the amorphous form.

This is not an ordinary inherency situation where it is not explicitly stated what the product actually is. Here the reference teaches exactly what the compound is. The only difference is a characteristic about which the reference happens to be silent. See also Ex parte Anderson, 21 USPQ 2nd 1241 at 1251, discussion of Rejection E. There, the decision states, "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at lease, in part determined by the precise process used in its manufacture. Page 1253. The "properties" branch of that statement applies here.

Applicant is reminded that the PTO has not testing facilities.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17 and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buhlmayer et al., U.S. Pat. Num. 5,399,578.

Claims 17 and 83 of Applicant's instant elected invention teaches an amorphous form of valsartan, wherein the amorphous form has a DSC thermogram that lacks a melting point above about 1 J/g and wherein the melting point is lacking in the region of from about 80°C to about 100°C.

Determination of the scope and content of the prior art (MPEP § 2141.01)

Buhlmayer teaches the amorphous form of valsartan. (See U.S. Pat. Num. 5,399,578, Claims 1-4). Bulmayer also teaches several melting intervals of valsartan: (1) 105°C -115°C from ethyl acetate ('578 Patent Example 16, Column 34, Line 62 and Instant application, page 3, lines 6-7).

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the prior art of Buhlmayer and the instant claims is that the prior art is silent as to the DSC thermogram, but it does teach that the melting point of amorphous valsartan is not in the region of about 80°C to about 100°C.

Finding of prima facie obviousness – rationale and motivation (MPEP § 2142-2413)

One skilled in the art would have found the claimed compound prima facie obvious because the instantly claimed compound and the compound in Buhlmayer are the same compounds, i.e. amorphous valsartan. Buhlmayer does not claim the DSC thermogram of amorphous valsartan. The absence of the DSC thermogram data does not necessarily mean that the DSC thermogram of amorphous valsartan is different. One skilled in the art may assume that

since the compounds are the same and the melting interval of the valsartan in Buhlmayer meets the criteria in Claim 18 of the instant application one skilled in the art would expect them to also share the same properties.

The DSC thermogram and melting points are highly dependent on the purity of the compound, type of solvent used and various other factors, as illustrated in Buhlmayer. For example, the melting interval of valsartan from ethyl acetate is 105°C-115°C (Column 34, line 62), while the valsartan from ethyl acetate in crystalline form has a melting interval of 105°C-1150°C (Column 49, line 52). In addition, different conditions such as concentration and temperature product different forms of valsartan that affect the melting interval. For example, the melting interval of a colourless crystal form of valsartan from ethyl acetate is 134°C-136°C (Column 58, line 11) and the melting interval of light brown crystals of valsartan from ethyl acetate and diethyl ether is 189°C-190°C (Column 58, line 43). It is well established that change in temperature, concentration, or both is not a patentable modification in the absence of unexpected results which is different in kind and not degree. In re Aller, 105 USPQ 233. In addition, discovery of an optimum value of a result effective variable is not patentable if such discovery is within skill in the art. A prima facie case of obviousness may be rebutted in optimizing a variable only when results are unexpectedly good. In re Boesch, 205 USPQ 215. Therefore, the claimed compounds are obvious in light of the prior art unless applicant can show that the difference in the DSC thermogram of the amorphous valsartan dramatically change the utility of the compound.

A prima facie case of obviousness may be rebutted by showing that the art, in any

material respect, teaches away from the claimed invention or has unexpected results, etc.... In the instant application, one skilled in the art would find that the prior art does not teach away, but rather teaches the instantly claimed invention and therefore, there are no unexpected results. Using the process outlined in the prior art the amorphous form of valsartan can be made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17 and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "above about" renders the claim indefinite because it is unclear what the scope of the claim is, for example is it 2 J/g, 5 J/g, 12 J/g, etc..., thereby rendering the scope of the claim unascertainable. Examples 1-13 (valsartan purely amorphous) of the specification, pages 25-28, state that there is no endothermic peak in some case, while in other cases the endothermic peak is not mentioned only that an X-ray analysis showed that it was purely amorphous indicating that the endothermic peak could be much greater than 1 J/g. Examples 14-19 and 29-31 (valsartan essentially amorphous) of the specification, pages 28-30 and 32 state that an endothermic peak could be seen at about 2 J/g, 3 J/g, 10 J/g, 12/g or in some cases the endothermic peak is not mentioned, which indicates it could be even greater than the values listed. In addition, it is unclear what the scope of the claim is, for example is the melting point below 80°C or is it above 100°C, does the melting temperature include 80°C and 100°C, etc..., thereby rendering the scope of the claim unascertainable.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17 and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims must stand alone to define the invention and incorporation into claims by express reference to the specification is not permitted. Ex parte Fressola, 27 USPQ 2d 1608. Claims that require one to read the specification to determine the metes and bounds of the invention are repugnant to modern practice in the Office and are properly rejected under 35 USC 112, 2nd paragraph, as failing to particularly point out and distinctly claim the invention. Id. At 1609.

Claim 17 is drawn to an amorphous form of valsartan, wherein the amorphous form has a DSC thermogram that lacks a melting point above about 1 J/g. Claim 83 is drawn to an amorphous valsartan having a DSC thermogram that lacks a melting enthalpy above about 1 J/g in region of about 80°C. to about 100°C. The claims are drawn to amorphous valsartan, but it unclear whether it is "purely amorphous" valsartan or "essentially amorphous" valsartan.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Chung whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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